AMENDMENT

Please amend the application as follows:

In the Specification:

Please replace the paragraph beginning at page 7, line 13 and ending at page 7, line 20 with the following amended paragraph:

Figure 2 shows the Novel Library vector described herein is a shuttle vector containing ampicillin and the colE1 origin of replication for selection in E.coli as well as TRP1 and the 2 micron origin of replication for selection in yeast. Unknown cDNAs are fused to the Gal4p activation domain, and continuously variable expression is obtained by the induction of GRE upstream activating element(s) attached to CYC1 promoter. AMP = Ampicillin, *E.coli* selectable marker; ori= colE1 bacterial origin of replication; TRP= TRP1 gene, yeast selectable marker; 2um= origin of replication for yeast; GRE= Glucocortocoid Response Element; CYC1p= CYC1 promoter from yeast; Gal4AD= Gal4 activation domain; AdhT= Alcohol dehydrogenase terminator.

Please replace the paragraph beginning at page 7, line 21 and ending at page 8, line 3 with the following amended paragraph:

Figure 3 shows the novel Bait vector in a shuttle vector containing kanamycin and the colE1 origin of replication for selection in E.coli as well as URA3 and the 2um origin of replication for selection in yeast. A known cDNA is fused to the Gal4p DNA binding domain, and continuously variable expression is obtained by the induction of ERE element(s) attached to

CYC1 promoter. KAN= Kanamycin, *E.coli* selectable marker; ori= colE1 bacterial origin of replication; URA= URA3 gene, yeast selectable marker; 2um= origin of replication for yeast; ERE= Estrogen Response Element; CYC1p= CYC1 promoter from yeast; Gal4pBD= Gal4p DNA binding domain; AdhT= Alcohol dehydrogenase terminator.

Please replace the paragraph beginning at page 8, line 4 and ending at page 8, line 10 with the following amended paragraph:

Figure 4 shows Continuously Dose Responsive Expression of proteins fused to Gal4pBD in the "Bait Vector" in yHYB001 strain. Strain yHYB001 with the bait vector is grown in selective minimal media with varying concentrations of estradiol. The bait vector contains the Gal4pBD fused to the marker *lacZ*. β-gal expression assays are performed three times per estradiol concentration; the data represents an averaging of three assays per sample. Growth was overnight and strains were at OD_{600} ca. 0.8 when assayed. Strain yHYB001 is described in the text. β-gal expression assays are described in Guarente (1983). The variable "n" in the x-axis label "Dose (10^{-n}) dexamethasone" represents any given number on the x-axis.

Please replace the paragraph beginning at page 8, line 11 and ending at page 8, line 17 with the following amended paragraph:

Figure 5 shows Continuously Dose Responsive Expression of proteins fused to Gal4pAD in the "Library Vector" in yHYB001 strain. Strain yHYB001 with the library vector is grown in selective minimal media with varying concentrations of dexamethasone. The library vector contains the Gal4pAD fused to the marker *lacZ*. β-gal expression assays are performed three times per dexamethasone concentration; the data represents an averaging of three assays per

sample. Growth was overnight and strains were at OD_{600} ca. 0.8 when assayed. Strain yHYB001 is described in the text. β-gal expression assays are described in Guarente (1983). The variable "n" in the x-axis label "Dose (10^{-n}) dexamethasone" represents any given number on the x-axis.

Please replace the paragraph beginning at page 17, line 19 and ending at page 17, line 25 with the following amended paragraph:

In this embodiment, in the first hybrid protein, the bait may be fused to the carboxyl-terminal end of the GAL4bd, a DNA binding domain (Figure 3). This first hybrid protein may be transcribed in a continuous range of amounts over up to five orders of magnitude , and under the influence of an estrogen response element (ERE) within a minimal promoter. This results in variable expression of the bait first hybrid protein over a continuous range of amounts in response to changing levels of estrogen or estrogen antagonists in the yeast growth medium. This promoter-first hybrid protein construct is provided on a two-micron plasmid either under ARG4 or URA3 selection.

Please replace the paragraph beginning at page 18, line 1 and ending at page 18, line 12 with the following amended paragraph:

The second hybrid protein may be formed by fusion of the prey polypeptide, which may be derived from a library, to the carboxyl-terminal end of the GAL4ad , a transcriptional activation domain (Figure 2). This second hybrid protein may be transcribed in a continuous range of amounts over up to five orders of magnitude and under the influence of preferably one to six, and in the present example, three, glucocorticoid response elements (GREs) within a

minimal promoter, for example, including but not limited to that from CYC1. This results in variable expression of the second hybrid protein over a continuous range of amounts in response to changing levels of glucocorticoids or their antagonists, including but not limited to dexamethasone, in the yeast growth medium. This promoter- second hybrid protein construct is provided on a two-micron plasmid under TRP1 selection. Both hybrid protein plasmids are also shuttle vectors containing either ampicillin or kanamycin resistance and a colE1 origin of replication, which provide for manipulation in *E. coli* bacteria.

Please replace the paragraph beginning at page 19, line 4 and ending at page 19, line 20 with the following amended paragraph:

As noted above, the Brent lab has shown that a given set of two-hybrid protein interactors yield a uniform quantitative reporter output directly proportional to their strength of interaction (Estojak et al., 1995). Utilizing the novel adjustable yeast interaction hybrid system (IHS), introduced and described as a more preferred embodiment in the paragraphs above, three sets of proteins pairs previously demonstrated to interact in a two-hybrid system are demonstrated to give variable levels of reporter output when expressed at different relative concentrations. The level of expression of the first hybrid protein containing the bait is proportional to the concentration of estradiol, and the level of the second hybrid protein containing the prey derived from a library is proportional to dexamethasone concentration (Kralli et al., 1995; Gaido et al., 1997 (Figures 4 and 5)).